Utilization of Coal Tar Bases

Francis E. Cislak

Reilly Tar & Chemical Corporation, Indianapolis, Indiana

The carbonization of coal gives rise to a complex mixture of hundreds of chemical compounds. Most of these compounds fall into one of three groups: hydrocarbons, acids, and bases. The coal tar bases are nitrogen compounds. The nitrogen atom is in the ring, as in pyridine, or it is attached to the ring as in aniline. Of the large number of compounds that are included in the category of coal tar bases, only pyridine and its simpler homologs are considered in this presentation.

Narrating the actual uses to which pyridines are put would be one way of discussing the utilization of coal tar bases. Perhaps a more stimulating approach is the one adopted herein, that is, a presentation of an outline of some chemical reactions of pyridines which are involved in their utilization.

Quaternization. Pyridine and the alkylpyridines react with alkyl halides, acid chlorides, and with alkyl or aryl sulfonic esters to form pyridinium salts. The rate of quaternization is influenced by the nature and position of the substituents on the pyridine ring. Methyl groups adjacent to the nitrogen decrease the rate of quaternization (127). The tendency to quaternize decreases in the order 4-picoline> 2-picoline> 2,4-lutidine> 2,6-lutidine. A method of purifying 2,6-lutidine from such contaminants as 3-picoline and 4-picoline, is based on the fact that 2,6-lutidine quaternizes much more slowly than do the picolines. The presence of a carboxyl group on the pyridine ring greatly retards the rate of quaternization. On the other hand, the esters of pyridine carboxylic acids are quaternized rather smoothly (118).

Pyridyl-pyridinium salts wherein the nitrogen atom of a pyridine nucleus is connected to a carbon atom at the 2-, 3-, or 4- position of a second pyridine molecule are known. N-pyridyl-4-pyridinium dichloride, made by the reaction of thionyl chloride upon pyridine (87) (21)(11), had been utilized in the preparation of 4- substituted pyridines (75). The recent contributions to the chemistry of pyridine-N-oxide have made N-pyridyl-4-pyridinium dichloride of less importance in the preparative methods (30).

2-Vinylpyridine reacts with pyridine hydrochloride to give an almost quantitative yield of 2-pyridylethylpyridinium chloride. The reaction is a general one, similar quaternary compounds are formed with pyridine thiocyanate, with quinoline hydrochloride, etc. 4-Vinylpyridine reacts in like manner (35).

Quaternary salts of pyridine, of alkylpyridines, as well as of other pyridine compounds may be oxidized by potassium ferricyanide to 1- substituted 2-pyridones (123). The nature of the substituent in the 3- position of a pyridinium salt determines whether ferricyanide oxidation gives a 2-pyridone or a 6-pyridone. If the 3- position is occupied by phenyl, 3-pyridyl, carboxy, or carboxy ethyl, 6-pyridones are formed. If the substituent is bromine, methyl, or ethyl, the oxidation occurs mainly at the 2- position. 3-Cyanopyridine methyl

iodide appeared to form both 2-, and 6-pyridones (22)(141). A more recent study of the ferricyanide oxidation of the quaternary of 1-phenylethyl-3-cyanopyridine does not confirm the presence of a 6-pyridone (144).

Methyl iodides of isonicotinic acid esters are oxidized with alkaline potassium ferricyanide to 4-carboxy-N-methyl-2-pyridone in yields up to 96% (55).

5-Alkyl-2-picolinium salts upon oxidation with iodine and pyridine and subsequently treating the resulting compound with dilute caustic give 1- substituted 5-alkyl-2-pyridones (14).

The pyridine-N-oxides also form quaternary compounds (82)(49). These compounds are important in the preparation of 2- and 4- substituted pyridines.

Oxidation. The inertness of pyridine towards oxidizing agents is one of its outstanding characteristics. Pyridine is not attacked by fuming nitric acid nor by chromic acid, and even potassium permanganate has but little effect on it.

In spite of its resistance to oxidation, pyridine may be oxidized quite readily to pyridine-N-oxide. The reaction is usually carried out with a mixture of hydrogen peroxide and acetic acid (67)(113)(115). The formation of the N-oxide linkage is a fairly general behavior of compounds containing the pyridine nucleus. Alkylpyridines form pyridine-N-oxides; so do alkanolpyridines (31)(17); and acetylpyridines (82)(129). Nicotinic acid, isonicotinic acid, and picolinic acids give the corresponding N-oxides (43)(59)(10), and so do their esters (82)(18), but 2,5-pyridine dicarboxylic acid is not oxidized to the N-oxide while its dimethyl ester is (118). The pyridine carboxamides also form N-oxides in the usual manner (57).

2-Bromopyridine-N-oxide and 2-bromo-6-methylpyridine-N-oxide are formed in good yields (3), and so are 3-bromopyridine-N-oxide and 3,5-dibromopyridine-N-oxide (57). 2-, 3-, and 4-pyridine sulfonic acids are resistant to oxidation by hydrogen peroxide and acetic acid. However, the sodium salts are readily converted to the corresponding N-oxides (47).

In contrast to the stability of pyridine, the alkylpyridines are attacked by a variety of oxidizing agents. The oxidation of the picolines, especially of the 3- and 4- isomers, to the corresponding pyridine carboxylic acids is one of their commercially more important reactions.

Potassium permanganate is used to convert the picolines to pyridine carboxylic acids (15)(98)(139). It is also useful in preparing 2-aminopyridine carboxylic acids from 2-aminopicoline (53) and 4-aminonicotinic acid from 4-amino-3-picoline (142). Potassium permanganate may be used to oxidize selectively a pyridine compound having more than one oxidizable group. An alkyl group in the 3- position is more readily oxidized than is one in the 4- position. 3,4,5-Trimethylpyridine oxidized with a 2% aqueous $KMnO_4$ gives 4,5-dimethylnicotinic acid and 4-methylnicotinic acid. 3,5-Dimethyl-4-butylpyridine forms 4-butyl-5-methylnicotinic acid and 4-butyl dinicotinic acid (148).

4-Methyl picolinic acid can be made from 2-styryl-4-methylpyridine by $KMnO_4$ oxidation at 0° to 5° C. (42); 4,5-diethyl picolinic acid from 2-styryl-4,5-diethylpyridine (91); 4-isopropyl-5-ethyl picolinic acid from 2-styryl-4-isopropyl-5-ethylpyridine (122). Treatment of 2-styrylpyridine at 200° C. with selenium dioxide gives 1-phenyl-2-(2-pyridyl)-1,2-ethane dione (24).

Nitric acid is an important commercial oxidizing acid. The picolines resist oxidation by nitric acid. Even at its boiling point nitric acid does not oxidize 3-picoline (121). Nitric acid at a temperature of about 230° C. and about 35 atms pressure oxidizes 3-

picoline to nicotinic acid (50% yield) and 4-picoline to isonicotinic acid (90% yield)(13).

A mixture of nitric acid and sulfuric acid or phosphoric acid gives good yields of pyridine carboxylic acids from picolines. The reaction proceeds at atmospheric pressures (39).

Sulfuric acid, with selenium as a catalyst, may also be used to oxidize picolines to pyridine carboxylic acids (155). The oxidation of 2,4-lutidine with sulfuric acid plus selenium gives 29% of 2,4-pyridine dicarboxylic acid and 18% of 2-methylisonicotinic acid (116).

Pyridine carboxylic acids can be produced by the catalytic vapor phase air oxidation of picolines (37). The position of the methyl group determines the ease of oxidation; the methyl group in the 3-position is the most resistant to oxidation (36).

Vapor phase oxidation of picolines with air in the presence of ammonia or an amine yields cyanopyridines. This method of making cyanopyridines was first observed in the vapor phase oxidation of nicotine wherein 3-cyanopyridine was made (38). 3-Picoline is converted to 3-cyanopyridine by oxidation with sulfur in the presence of ammonia (143).

Recent studies on the oxidation of picolines with selenium dioxide show the ease of oxidation to be 4-picoline> 2-picoline> 3-picoline. In fact, 3-picoline is not affected by SeO_2 and hence is used as a solvent for carrying out the oxidation of the other picolines. 2,5-Lutidine gives 79% of 3-methyl picolinic acid. 2,4-Lutidine gives a mixture of 2-methyl isonicotinic acid (44%) and 2,4-pyridine dicarboxylic acid (76).

Picolinic acid has been prepared by the liquid phase oxidation of 2-picoline with gaseous oxygen in the presence of a copper salt of a fatty acid (65); similarly isocinchomeronic acid was made from aldehyde collidine and isonicotinic acid from 4-picoline (134).

3-Picoline has been oxidized electrolytically to nicotinic acid (89).

Alkylpyridines may be oxidized to the corresponding aldehydes by vapor phase oxidation in the presence of a large excess of water vapor. 2-Picoline gives 2-pyridine aldehyde (106); 2,6-lutidine may give 6-methyl2-pyridine aldehyde, 2,6-pyridine dialdehyde (107) and 6-carboxy-2-pyridine aldehyde (103); 3,5-lutidine forms 5-methyl-3-pyridine aldehyde (105).

It has been reported that 2-picoline may be oxidized to 2-pyridine aldehyde by means of selenium dioxide (99)(66)(20).

Useful laboratory methods for the preparation of pyridine aldehyde involve the oxidation of pyridyl carbinols with manganese dioxide (64), selenium dioxide (77), or lead tetracetate (111). 2,6-bis-Hydroxymethylpyridine is oxidized by SeO_2 to 2-hydroxymethyl-6-pyridine aldehyde (104). The 3-pyridylaldehyde has been prepared by vapor phase oxidation of 3-pyridyl carbinol (69).

3-Pyridine aldehyde, 4-pyridine aldehyde, and 6-methyl-3-pyridine aldehyde were prepared in good yield by reducing 3-cyanopyridine, 4-cyanopyridine, and 6-methyl-3-cyanopyridine with semi-carbazide hydrochloride and Raney Nickel, and liberating the aldehyde from the resulting aldehyde semicarbazone by acid hydrolysis in the presence of meta nitrobenzaldehyde (50). 3-Pyridine aldehyde in 83% yield has also been made by the reduction of 3-cyanopyridine with $NaHAl(OEt)_3$ (73).

Isonicotinaldehyde has been made by the ozonization of 4-styrylpyridine (152); 2-pyridine aldehyde by the ozonization of 2-vinylpyridine (25).

Hydrogenation. In contrast to its inertness towards oxidation, pyridine is rather easily hydrogenated. The complete reduction of

pyridine to piperidine, i.e. its hexahydro derivative, is a commercial operation of many years standing.

Various catalysts are useful in reducing pyridine with hydrogen. Nickel catalysts, especially Raney Nickel, are suitable for the formation of piperidine (5). To avoid hydrogenolysis with the formation of high-boiling by-products, the temperature is kept as low as possible (78). The alkylpyridines are readily reduced by hydrogen (Raney Nickel catalyst) to the corresponding alkylhexahydropyridines (5)(130)(80).

Platinum oxide is a useful catalyst for the laboratory hydrogenation of pyridines. Pyridine poisons platinum oxide catalyst. However, the hydrogenation of pyridine hydrochloride, or of quaternary salts of pyridine proceeds very well (61). The slow rate of hydrogenation of the base itself may be due to the free electrons on the nitrogen. Through these electrons the pyridine forms a compound with the catalyst thereby withdrawing the platinum from its role of a catalyst. In the quaternary salts, the pyridine electrons are tied up, thereby permitting the hydrogenation to proceed many times faster than if free pyridine were used (108). The pyridine when dissolved in acetic acid can be hydrogenated with platinum oxide (54).

Piperidine manufactured by the electrolytic reduction of pyridine contains substantial quantities of tetrahydropyridine; the piperidine produced by hydrogenation over Raney Nickel contains no appreciable amount of the 1,2,5,6-tetrahydropyridine (45). Electrolytic reduction of 2-methylpyridine gives 2-methylpiperidine and 24.4% of 2-methyl-1,2,3,6-tetrahydropyridine; 3-methylpyridine gives 3-methyl-1,2,5,6-tetrahydropyridine in addition to 3-methylpiperidine; and 4-methylpyridine gives 4-methylpiperidine and 4-methyl-1,2,3,6-tetrahydropyridine (51). The electrolytic reduction of quaternary pyridinium salts gives the same types of products so far as the position of the double bond is concerned (52).

In the laboratory, sodium and absolute alcohol are frequently used to reduce pyridine to piperidine (102). This reaction was discussed in 1884 by Ladenburg (90). It is important that the alcohol be dry. If 95% ethanol is used, little or no piperidine is produced but instead the pyridine ring is ruptured and ammonia evolved (136)(137). Reducing 3-methylpyridine with sodium and absolute butanol gives in addition to 3-methylpiperidine, 28.4% of 3-methyl-1,2,5,6-tetrahydropyridine; 4-methylpyridines gives 45% of 4-methyl-1,2,3,6-tetrahydropyridine in addition to 4-methylpiperidine (51). A number of 4-alkylpiperidines were prepared from 4-alkylpyridines by reduction with sodium and butanol followed by hydrogenation with hydrogen in the presence of palladium. The sodium-butanol reduction gave mainly the tetrahydropyridine which was converted to the piperidine by hydrogen (149).

Reduction of pyridine with $LiAlH_4$ gives 1,2-dihydropyridine (19). $LiAlH_4$ reduction of quaternary salts of alkylpyridines gives only the tetrahydropyridines (51).

Pyridine carboxylic acid esters are reduced, in good yield, by $LiAlH_4$ to the corresponding hydroxymethylpyridines (79)(112)(81); but their quaternaries with $LiAlH_4$ give 1-alkylhydroxymethyl-tetrahydropyridines (51).

Catalytic hydrogenation (Ni catalyst) of pyridine in various aliphatic alcohols (1 to 16 carbon atoms) gives the corresponding 1-alkylpiperidine in yields in excess of 70% (133).

Amination. Because of the difficulty of nitrating pyridine, the usual methods for the synthesis of aromatic amines are not available for the preparation of aminopyridines. The nitration of pyridine proceeds only under drastic conditions, fuming sulfuric acid and potassium nitrate plus a temperature in excess of 300° C.; the nitro group enters

the 3- position; the yield is only 15% (84). When especially high temperatures are used, the nitro group occupies the 2- position (46). Poly-alkylpyridines are somewhat easier to nitrate, the reaction conditions are milder, and the yields are better (120).

While pyridine is difficult to nitrate, pyridine-N-oxide is readily nitrated; the nitro group enters the 4- position (115). The nitration can be carried out at water-bath temperatures with a mixture of nitric and sulfuric acids; the yield is above 80% (83). The ease of nitration extends to the alkylpyridine-N-oxides and to various derivatives of pyridine-N-oxide.

The 4-nitropyridine-N-oxides are readily reduced and deoxygenated to the corresponding 4-aminopyridines. Various reducing agents have been used, e.g. iron and acetic acid (115), hydrogen with Raney Nickel (41)(63), hydrogen with palladium in acetic anhydride (48). 4-Nitropyridine-N-oxides offer a good route to 4-aminopyridines.

Prior to the 4-nitropyridine-N-oxide approach to the synthesis of 4-aminopyridine, it was prepared by the Hofmann degradation of isonicotinamide (93)(114) or from 4-pyridyl pyridinium dichloride and ammonium hydroxide (87)(6). The latter method has also been used for making 4-amino-3-methylpyridine (44).

The most convenient method for preparing 3-aminopyridine is from nicotinamide (7); it may also be prepared from 3-bromopyridine and aqueous ammonia in the presence of copper sulfate (97).

In 1914 the Russian chemist, Chichibabin, discovered a most interesting and useful reaction for introducing an amino group onto the 2- position of the pyridine nucleus. He found that pyridine reacts with sodamide to form 2-aminopyridine (92). The amino group goes almost exclusively into the 2- position, only a trace of 4-aminopyridine is formed; no 3-aminopyridine is found.

2-Aminopicolines may be prepared by reacting the picolines with sodamide (135). In the case of 3-picoline, the two carbon atoms adjacent to the nitrogen are different because of their relation to the 3-methyl group. Sodamide gives two aminopicolines when it is reacted with 3-picoline, that is, 2-amino-3-picoline and 6-amino-3-picoline; the former predominates (34).

Pyridine and 2-picoline have been aminated in the alpha position with alkylamines by refluxing the pyridine with a slight excess of the alkylamine and a stoichiometric amount of sodium (88).

Alkylation. There are several interesting reactions available for the alkylation of the pyridine ring. Arens and Wibaut found that an alkyl group may be introduced onto the 4- position of pyridine by the action of zinc dust on a mixture of pyridine, an organic acid anhydride and the corresponding organic acid (9)(56). This reaction is not applicable to alpha substituted pyridines; it cannot be used to introduce an alkyl group onto the 4- position of 2-picoline, 2-aminopyridine, picolinic acid, nor of 2-chloropyridine (153). The reaction proceeds in a "normal" manner with 3-picoline (140). Iron powder may be used in place of zinc dust (154).

At the Reilly Laboratories we found that pyridine as well as alkylpyridines may be alkylated by the use of aliphatic acid salts of tetravalent lead (128). By this means alkyl groups containing one less carbon atom than the acid radical of the lead salt are produced; the alkyl group enters both the 2- and the 4- positions if they are open. The reaction of 3-butylpyridine with lead tetra-acetate gives a mixture of 3-butyl-2-methylpyridine (15%), 5-butyl-2-methylpyridine (5%), 3-butyl-2,6-dimethylpyridine (1.5%), and 3-butyl-4-methylpyridine (5%) (62).

Lithium alkyls and phenyl lithium are used to introduce an alkyl or phenyl group onto the 2- position of pyridine (156), of 3-picoline

(1), of 3-aminopyridine and 3-methoxypyridine (2).

In 1936 Chichibabin described the alkylation of 2-picoline and of 4-picoline by reacting the picolines with sodamide to form picolylsodium and reacting the latter compound with an alkyl halide (29). The activity of the hydrogen atoms in the methyl groups of 2- and 4-picoline is ascribed to the ability of these picolines to take part in resonance with the azomethine linkage of the pyridine ring. Since 3-picoline cannot participate in such resonance, it was long believed that 3-picoline could not be alkylated by the Chichibabin method. In 1951 Brown and Murphey (23) showed that 3-picoline may be alkylated by the sodamide method.

The Chichibabin method of alkylating picolines is of general applicability, both the lower alkyl halides as well as long chained ones may be used (86). Substituted picolines may be alkylated (101)(8)(132)(26).

2,4,6-Collidine presents an opportunity of attaching an alkyl group on either of the alpha methyl groups or onto the methyl group in the 4- position. We found that the sodamide method introduces the alkyl onto the 4-methyl group (33). 2,4-Lutidine is also alkylated at the 4- position (95).

Ziegler and Zeiser (156) showed that phenyl-lithium reacts with 2-picoline to form 2-picolyl-lithium which may be reacted with alkylhalides to attach an alkyl group onto the 2-methyl group. This reaction has been applied to the preparation of a number of 2-picolyl compounds. With 2-bromopyridine there is formed 2,2'-dipyridylmethane (117). With chloroacetylenes, 2-pyridylacetylenes are prepared (58). 1-(2-Pyridyl)-4-chloro-3-pentene was made from 1,3-dichloro-3-butene (72). 2-Pyridylmalondinitrile was made from N-methyl-N-cyanoaniline (94).

In contrast to the ease of introducing groups onto the 4-methyl group through the intervention of sodamide, attempts to use the lithium method have not been too satisfactory (117). The usual manner of making 2-picolyl-lithium is to prepare a solution of phenyl lithium and then add 2-picoline to this solution. In the alkylation of 4-picoline, better results are obtained when the phenyl-lithium is added very slowly to the 4-picoline (151).

Alkylation of 2,4,6-collidine by the sodamide process proceeds mainly at the 4- position. Alkylation by the lithium method gives mainly 2,6-dialkyl-4-methylpyridine and a lesser amount of 2,4,6-trialkylpyridine (74).

Alkali metals are used as catalysts in the alkylation of 2-picoline and 4-picoline with compounds containing an ethylenic double bond. A mixture of 2-picoline, sodium, and ethylene under 60 atms. pressure heated to 120-130° gives a mixture of 2-propylpyridine (23%) and 2-(3-pentyl)pyridine (126)(119). Under similar conditions 2-picoline and butadiene give 2-(3-pentenyl)pyridine and 2-(5-nondienyl-2,7)pyridine; styrene and 2-picoline give 1-phenyl-3-(2-pyridyl)propane (150). Acrylonitrile reacts with 2- and 4-picolines in the presence of a bit of sodium to give pyridyl-butyronitriles and dicyanopyridyl pentanes (32)(26).

Picolines with methyl groups in the 2- or 4- position may be alkylated in the vapor phase by reaction with aliphatic aldehydes (40).

Condensation. The reaction of picolines with aldehydes may be considered a classic in the pyridine series. The methyl groups in the 2- and the 4- position are reactive, whereas a methyl group in the 3- position is not.

2-Picoline condenses with formaldehyde to give 2-ethanolpyridine (85); 4-picoline gives 4-ethanolpyridine (124).

2,4,6-Collidine presents a situation wherein the formaldehyde

must decide whether it will react with the methyl group in the 4-position or with one of the alpha methyl groups. In the presence of a large excess of 2,4,6-collidine, the formaldehyde condenses almost exclusively with a methyl group in the 2- position; only a trace of the 4-ethanolpyridine is formed (109). In the presence of a large excess of formaldehyde, the 4-methyl group as well as both alpha methyl groups react (96)(16). 2,4-Lutidine also reacts with formaldehyde, preferentially at the 2- position (110)(42).

4-Ethylpyridine has been condensed with formaldehyde (excess) to give a mixture of dimethylol-4-ethylpyridine (65.5%) and of monomethylol-4-ethylpyridine (26.6%)(131).

The introduction of the -N-oxide group enhances the activity of picolines towards condensation reactions. Neither 2- nor 4-picoline will condense with ethyl oxalate, but their -N-oxides readily condense with ethyl oxalate to give the corresponding pyruvates (4).

Studies in our laboratory show that the presence of a chlorine in the 2- position of 4-picoline retards the condensation activity of the methyl group. 4-Bromo-2-picoline reacted with formaldehyde to give only a 9% yield of the corresponding ethanolpyridine (125).

To improve the yield of 2-(2-hydroxyethyl)-3-picoline, the 2-lithio derivative of 2,3-lutidine was reacted with paraformaldehyde. 2-Picolyl-lithium reacts smoothly to give 2-ethanolpyridine (54). 2,6-Lutidine through its 2-lithio derivative has been condensed with propionaldehyde to give a good yield of 2-(2-hydroxybutyl)-6-methylpyridine (68).

2-Picoline and 4-picoline readily condense with benzaldehyde and with substituted benzaldehydes. With benzaldehyde, it is difficult to stop the reaction at the ethanol stage because of the ease with which this alkine dehydrates to stilbazole. If it is desired to stop at the alkine stage, it is suggested that the picoline be condensed with the benzaldehyde in the presence of water and that no condensing agent be used (138). The yield of alkine is increased by replacing a hydrogen of the methyl group of 2-picoline with magnesium and condensing the resulting 2-picolyl magnesium chloride with benzaldehyde (100).

Stilbazoles are the products usually obtained by the condensation of aromatic aldehydes and 2-picoline and 4-picoline. In general, the reaction is carried out by refluxing a solution of the aromatic aldehyde, the picoline, and acetic anhydride (138)(28)(60). Yields above 90% are not uncommon (71).

Since 3-picoline does not condense with aldehydes, 3-stilbazole cannot be made as are the 2- and 4-stilbazoles. 3-Stilbazole has been made by condensing 3-pyridyl acetic acid with benzaldehyde and then decarboxylating the resulting beta-phenyl-alpha-3-pyridyl acrylic acid (12). The methyl iodide quaternary of 3-picoline condenses with benzaldehyde in the presence of piperidine to give a small yield of the alkine (75).

Benzaldehyde condenses with 2,4-lutidine by adding a molecule of the aldehyde to each of the methyl groups to give 2,4-distyrylpyridine (60)(110) and also to give 2-styryl-4-methylpyridine (42). 2,6-Lutidine condenses with benzaldehyde to give a mixture of 2-methyl-6-styrylpyridine and 2,6-distyrylpyridine (70).

The hydrogens of the methyl groups in 2- and 4-picoline are comparable in reactivity to those of the methyl ketones. And, as would be expected, the Mannich reaction applies to these compounds. 2-Picoline condenses with formaldehyde and diethylamine to give 2-(beta-diethylaminoethyl)pyridine (145).

Formaldehyde in an alkaline medium reacts with 3-hydroxypyridine to yield 2-hydroxymethyl-3-hydroxypyridine (146); 2-methyl-5-hydroxypyridine gives 2-methyl-5-hydroxy-6-hydroxymethylpyridine, indicating the influence of the hydroxyl group is more dominant than that of the

alpha methyl group (147). With benzaldehyde, 2-methyl-3-hydroxypyridine in an acid medium gives 2-styryl-3-hydroxypyridine (75).

Bibliography

1. Abramovitch, Giam-Choo Seng, and Notation, Can. J. Chem. 38, 761-71 (1960)
2. Abramovitch and Notation, Can. J. Chem. 38, 1445-8 (1960)
3. Adams and Reifschneider, J. Am. Chem. Soc. 79, 2236-39 (1957)
4. Adams and Schrecker, J. Am. Chem. Soc. 71, 1186-95 (1949)
5. Adkins, Kuick, Farlow, and Wojcik, J. Am. Chem. Soc. 56, 2425-28 (1934)
6. Albert, J. Chem. Soc. 1951, 1376
7. Allen and Wolf, Organic Syntheses, 30, 3-4 (1950)
8. Arata and Achuva, C.A. 53, 10211 (1959); Yakugaku Zasski 79, 108-10 (1959)
9. Arens and Wibaut, Rec. trav. chim., 61, 59-68 (1942)
10. Bain and Saxton, J. Chem. Soc., 1961, 5216-23
11. Bak and Christensen, C.A. 49, 4640-1 (1955); Acta chem. scand. 8, 390 (1954)
12. Beard and Katritzky, Rec. trav. chim. 78, 592 (1959)
13. Bengtsson, Acta Chem. Scand. 9, 832-6 (1955)
14. Berson and Cohen, J. Am. Chem. Soc. 78, 416-8 (1956)
15. Black, Depp, and Corson, J. Org. Chem. 14, 14-21 (1949)
16. Bodalski and Michalski, Bull. acad. polon. sci., Ser. sci. chim. 8, 217-18 (1960); C.A. 55, 18721 (1961)
17. Boekelheide and Feely, J. Org. Chem. 22, 589-92 (1957)
18. Boekelheide and Lehn, J. Org. Chem. 26, 428-30 (1961)
19. Bohlmann, Chem. Ber., 85, 390-4 (1952)
20. Borsche and Hartman, Ber. 73, 839-42 (1940)
21. Bowden and Green, J. Chem. Soc. 1954, 1795-8
22. Bradlow and Vanderwerf, J. Org. Chem. 16, 73-83 (1951)
23. Brown and Murphey, J. Am. Chem. Soc. 73, 3308-12 (1951)
24. Buehler, Harris, and Arendale, J. Am. Chem. Soc. 72, 4953-5 (1950)
25. Callighan and Wilt, J. Org. Chem. 26, 4912-14 (1961)
26. Carelli, C.A. 56, 4720-1 (1962); Ann. Chim. (Rome) 51, 713-18 (1961)
27. Cathcart and Reynolds, J. Am. Chem. Soc. 73, 3504 (1951)
28. Chiang and Hartung, J. Org. Chem. 10, 21-25 (1945)
29. Chichibabin, Bull. Soc. Chim. (5) 3, 1607-32 (1936)
30. Cislak, Ind. & Eng. Chem. 47, 800-2 (1955)
31. Cislak, U. S. Patent 2,735,851, February 21, 1956
32. Cislak, U. S. Patents 2,868,294 and 2,868,295, January 13, 1959
33. Cislak, Karnatz, and Kelley, U. S. Patent 2,505,461, April 25, 1950
34. Cislak and Kranzfelder, U. S. Patent 2,456,379, December 14, 1948
35. Cislak and Sutherland, U. S. Patent 2,512,789 (1950)
36. Cislak and Wheeler, U. S. Patent 2,300,741, November 3, 1942
37. Cislak and Wheeler, U. S. Patent 2,437,938, March 16, 1948
38. Cislak and Wheeler, U. S. Patent 2,456,380, December 14, 1948
39. Cislak and Wheeler, U. S. Patent 2,522,163, September 12, 1950
40. Cislak and Wheeler, U. S. Patent 2,786,846, March 26, 1957
41. Clark-Lewis and Singh, J. Chem. Soc. 1962, 2379-82.
42. Clemo and Gourlay, J. Chem. Soc. 1938, 478-79
43. Clemo and Koenig, J. Chem. Soc. 1949, Suppl. Issue No. 1, S231-2
44. Clemo and Swan, J. Chem. Soc. 1948, 198-200
45. Davies and McGee, J. Chem. Soc. 1950, 678-80
46. Den Hertog and Overhoff, Rec. trav. Chim. 49, 552-6 (1930)
47. Evans and Brown, J. Org. Chem. 27, 1329-36 (1962)
48. Evans and Brown, J. Org. Chem. 27, 1665-7 (1962)
49. Feely and Beavers, J. Am. Chem. Soc. 81, 4004-7 (1959)
50. Felder and Pitre, C.A. 52, 379 (1958); Gazz. chim. ital. 86, 386-91 (1956)

51. Ferles, C.A. 52, 13724-5 (1958); Chem. Listy 52, 668-73 (1958)
52. Ferles, C.A. 52, 13724-5 (1958); Chem. Listy 52, 674-81 (1958)
53. Ferrari and Marcon, C.A. 53, 7162 (1952); Farmaco (Pavia) Ed. Sci. 13, 485-9 (1958)
54. Finkelstein and Elderfield, J. Org. Chem. 4, 365-75 (1939)
55. Frank and Mosher, J. Org. Chem. 24, 196-8 (1959)
56. Frank and Smith, Organic Syntheses 27, 38-40 (1947)
57. Gardner, Wenis, and Lee, J. Org. Chem. 22, 984-6 (1957)
58. Gautier, Marszak, and Miocque, Bull. soc. chim. France, 1958, 415-18
59. Ghigi, Ber., 75, 1316-23 (1942)
60. Gilman and Karmas, J. Am. Chem. Soc. 70, 2809-10 (1948)
61. Hamilton and Adams, J. Am. Chem. Soc. 50, 2260-3 (1928)
62. Hardegger and Nikles, Helv. Chim. Acta, 40, 2421-7 (1957)
63. Hayashi, Yamanoka, and Shimizia, Chem. Pharm. Bull, (Tokyo) 6, 323 (1958); C.A. 53, 375-6 (1959)
64. Heinert and Martell, J. Am. Chem. Soc. 81, 3933-43 (1959)
65. Henke, Benner, and Scott, U. S. Patent 2,267,734, December 30,1941
66. Henze, Ber. 67, 750-3 (1934)
67. Hertog and Combe, Rec. trav. chim., 70, 581-90 (1951)
68. Hnevsova and Ernest, C.A. 54, 13115 (1960); Collection Czech. Chim. Communs. 25, 748-55 (1960)
69. Hoffmann-LaRoche, Swiss Patent 286,108, February 2, 1953; C.A. 48, 8271 (1954)
70. Horak and Stanek, C.A. 45, 6201 (1951); Chem. Listy 44, 310-11 (1950)
71. Horwitz, J. Org. Chem. 21, 1039-41 (1956)
72. Hudlicky and Mares, C.A. 52, 4628 (1958); Chem. Listy 51, 1875-9 (1957)
73. Husse and Schroedel, C.A. 51, 11341 (1957); Angew. Chem. 68, 438-9 (1956)
74. Iida, J. Pharm. Soc. Japan, 82, 150-56 (1962)
75. Jerchel, Fischer, and Thomas, Chem. Ber. 89, 2921-33 (1956)
76. Jerchel, Heider, and Wagner, C.A. 53, 5263-4 (1959); Ann. 613, 153-70 (1958)
77. Jerchel, Heider, and Wagner, Ann 613, 180-4 (1958)
78. Jones, J. Chem. Soc. 1950, 1392-7
79. Jones and Kornfeld, J. Am. Chem. Soc. 73, 107-9 (1951)
80. Jones and Lindsey, J. Chem. Soc. 1952, 3261-4
81. Karrer and Mainoni, C.A. 46, 6127 (1952); Helv. chim. acta 34, 2151-4 (1951)
82. Katritzky, J. Chem. Soc. 1956, 2404-8
83. Katritzky, Randall, and Sutton, J. Chem. Soc. 1957, 1769-75
84. Kirpal and Reiter, Ber. 58, 699-701 (1925)
85. Kitchen and Hanson, J. Am. Chem. Soc., 73, 1838-9 (1951)
86. Knight and Shaw, J. Chem. Soc., 1938, 682-3
87. Koenigs and Greiner, Ber. 64, 1049-56 (1931)
88. Kovacs and Vajda, Chem. & Ind. 1959, 259; C.A. 57, 5892 (1962)
89. Kulka, J. Am. Chem. Soc., 68, 2472-3 (1946)
90. Ladenburg, Ber. 17, 156 and 388-91 (1884)
91. Lee and Swan, J. Chem. Soc. 1956, 771-5
92. Leffler in Organic Reactions, Adams, Ed. John Wiley and Sons, Inc. New York, 1942, Vol. I, pp 91-104
93. Leis and Curran, J. Am. Chem. Soc. 67, 79-81 (1945)
94. Lettre, Jungmann, and Salfeld, Chem. Ber. 85, 397-407 (1952)
95. Lochte and Cheavens, J. Am. Chem. Soc. 79, 1667-9 (1957)
96. Lukes and Galik, Chem. Listy 51, 2319-24 (1957); C.A. 52, 6347 (1958)
97. Maier-Bode, Ber. 69, 1534-7 (1936)
98. Malan and Dean, J. Am. Chem. Soc. 69, 1797-8 (1947)
99. Marcot and Polland, C.A. 53, 18029 (1959); Compt. rend. 248, 252-4 (1959)

100. Marekov, C.A. 52, 18418 (1958); Comp. rend. acad. bulgare sci. 9, 35-8 (1956)
101. Marion and Cockburn, J. Am. Chem. Soc., 71, 3402-4 (1949)
102. Marvel and Lazier, Organic Syntheses, Coll. Vol. I, 93-95 (1932)
103. Mathes and Sauermilch, Ber. 87, 1868-9 (1954)
104. Mathes and Sauermilch, Ber. 89, 1515-21 (1956)
105. Mathes and Sauermilch, Ber. 93, 286-88 (1960)
106. Mathes, Sauermilch, and Klein, Ber. 84, 452-58 (1951)
107. Mathes, Sauermilch, and Klein, Ber. 86, 584-88 (1953)
108. Maxted, J. Soc. Chem. Inc. 67, 93-97 (1948)
109. Melichar, Chem. Ber. 88, 1208-10 (1955)
110. Michalski and Studniorski, Chem. Tech. (Berlin) 9, 96-7 (1957) C.A. 51, 10530 (1957)
111. Micovic and Mihailovic, Rec. trav. chim. 71, 972-6 (1952)
112. Mosher and Tessieri, J. Am. Chem. Soc, 73, 4925-7 (1951)
113. Mosher, Turner, and Carlsmith, Organic Syntheses 33, 79-81 (1953)
114. Murray and Langham, J. Am. Chem. Soc. 74, 6289-90 (1952)
115. Ochiai, J. Org. Chem. 18, 534-51 (1953)
116. Ochiai and Okuda, J. Pharm. Soc. Japan, 70, 156-61 (1950); C.A. 44, 5878 (1950)
117. Osuch and Levine, J. Am. Chem. Soc. 78, 1723-5 (1956)
118. Peterson, J. Org. Chem. 25, 565-9 (1960)
119. Pines, J. Am. Chem. Soc. 81, 2568 (1959)
120. Plazek, Ber. 72, 577-81 (1939)
121. Plazek and Kozdrojowna, Roczniki Chem. 25, 509-13 (1951) C.A. 48, 5863 (1954)
122. Prasad and Swan, J. Chem. Soc. 1958, 2024-38
123. Prill and McElvain, Organic Syntheses, Coll. Vol. II, 419-21 (1943)
124. Profft, Chem. Tech. (Berlin) 8, 378-82 (1956); C.A. 51, 4374 (1957)
125. Profft and Richter, C.A. 54, 11019 (1960); Wiss. Z. Tech. Hochsch. Chem. Leuna-Merseburg 2, 85 (1959-60)
126. Profft and Schneider, Arch. Pharm. 289, 99-104 (1956); C.A. 51, 402 (1957)
127. Reynolds and Kenyon, J. Am. Chem. Soc. 72, 1593-6 (1950)
128. Rieger, U. S. Patent 2,502,174, March 28, 1950
129. Risaliti and Lolli, Farmaco (Pavia) Ed. sci, 12, 705-11 (1957); C.A. 52, 11038 (1958)
130. Robinson, J. Org. Chem. 16, 1911-19 (1951)
131. Rubstov, Nikiskaya, and Usovskaya, Zhur. Obshchei, Khim. 25, 2453-7 (1955); C.A. 50, 9401 (1956)
132. Sato, Chem. & Pharm. Bull. (Japan) 7, 241-7 (1959)
133. Sawa, Inoue, and Kitamura, C.A. 45, 2940 (1951); J. Pharm. Soc. Japan 63, 319-25 (1943)
134. Schwarz, C.A. 53, 18970 (1957); Ger. 1,010,524, June 19, 1957
135. Seide, Ber. 57, 791-6 (1924)
136. Shaw, J. Chem. Soc, 125, 1930-4 (1924)
137. Shaw, J. Chem. Soc, 127, 215-6 (1925)
138. Shaw and Wagstaff, J. Chem. Soc. 1933, 77-79
139. Singer and McElvain, J. Am. Chem. Soc. 57, 1135-7 (1935)
140. Solomon, J. Chem. Soc. 1946, 934-6
141. Sugasawa and Kirisawa, Pharm. Bull. (Japan), 3, 187-9 (1955); C.A. 50, 8636 (1956)
142. Taylor and Crovetti, J. Org. Chem. 19, 1633-40 (1954)
143. Toland, J. Org. Chem. 27, 869-72 (1962)
144. Tomisawa, J. Pharm. Soc. Japan 79, 1173-6 (1959)
145. Tseon, Compt. rend. 192, 1242 (1931); C.A. 25, 4270 (1931)
146. Urbanski, J. Chem. Soc. 1946, 1104-5
147. Urbanski, J. Chem. Soc. 1947, 132-4
148. Vaculik and Kuthan, C.A. 54, 18506 (1960); Collection Czechoslov. Chem. Communs. 25, 1591-5 (1960)

149. Wawzonek, Nelson, and Thelen, J. Am. Chem. Soc. 74, 2894-6 (1952)
150. Wegler and Pieper, Chem. Ber. 83, 6-10 (1950)
151. Wibaut and Hey, Rec. trav. chim. 72, 513-21 (1953)
152. Wibaut, Kooyman, and Boer, Rec. trav. chim. 64, 30-4 (1945)
153. Wibaut and Vromen, Rec. trav. chim. 67, 545-50 (1948)
154. Wilbert, Reich, and Tenenbaum, J. Org. Chem. 22, 694-5 (1957)
155. Woodward, Badgett, and Kaufman, Ind. Eng. Chem. 36, 544-6 (1944)
156. Ziegler and Zeiser, Ber. 63, 1847-51 (1930)